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FIRST KNOWN OUTBREAK OF COLONIZING VANCOMYCIN-RESISTANT ENTEROCOCCI IN QUEBEC

Introduction

Vancomycin-resistant enterococci (VRE) are a threat to public health, particularly because clinical infections linked to vancomycin resistance are difficult or impossible to treat, and the mechanism that leads to VRE can be transmitted to other more virulent bacteria such as *Staphylococcus aureus*⁽¹⁾.

VRE first appeared in the United States in 1988. From 1989 to 1993, the rate of hospital-acquired infections due to VRE rose from 0.3% to 7.9%⁽²⁾. The first documented outbreak in Canada occurred in the fall of 1995 at a Toronto university hospital⁽³⁾.

This report describes the first known outbreak of colonizing VRE in Quebec, which occurred in a Montérégie hospital on the southwest shore of Montreal. Between September and December 1996, 20 cases were identified. There were no cases of infection.

Background

The *Centre hospitalier régional du Suroît* (CHRS) is a general and specialized care institution located in Montérégie. Of its 314 beds, 249 are for acute care and 65 are for extended care. The beds are located on two adjoining sixth- and eighth-floor wings (Y and Z), connected by passages in the basement and between floors G and H. Table 1 describes the services on each floor of the two wings.

The first case of VRE colonization occurred in an 80-year-old woman admitted for a dislocated shoulder. She was on long-term corticotherapy due to rheumatoid arthritis. Two days following her admission to hospital, she developed an abscess on the right buttock, accompanied by incontinence and confusion. Seven days following admission, a sample from the abscess was cultured. A preliminary report 2 days later indicated VRE. The patient was placed in isolation; prior to that, she had spent time on four different patient-care floors and also in the observation room of the emergency ward. The abscess cleared up following drainage.

The second case of VRE colonization occurred in an 84-year-old woman suffering from diabetes mellitus, atherosclerosis, and dementia. She was admitted for cellulitis of the left upper arm. Two days following admission, the patient experienced burning upon miction; a few days later, a urine culture indicated more than two types of microorganisms including VRE. Her urinary symptoms resolved following treatment with cloxacillin, which had begun upon admission to hospital for cellulitis.

These two cases had shared the same hospital room on floor A a few days apart. Screening other patients who had shared the room and who were still hospitalized revealed a third case of VRE colonization. The Infection Prevention Team of the CHRS, with the cooperation of the *Laboratoire de santé publique du Québec* (LSPQ) and the *Direction régionale de la santé publique de la Montérégie* (DRSP-M), began an investigation. An active surveillance for possible VRE carriers and of their environment was undertaken. Information was collected to determine any possible risk factors linked to acquiring VRE. Finally, strict control measures were put into place to prevent the spread of VRE within the hospital and in the community at large.

Method

To identify other possible cases of VRE colonization, six rounds of screening were conducted in the hospital. The first time, rectal swabs were taken from all patients, including those in acute and extended care. The second time, only acute-care patients were screened because no cases of VRE colonization had been discovered among those in extended care. Patients on the floors where carriers had been identified during prior screening were targeted the next three times. The final screening involved only patients on the floor where the positive cases were isolated. In addition, patients at risk of carrying VRE from the community or from another institution were screened and placed in preventive isolation while waiting for results. As a further precaution, patients hospitalized during the previous year in any other hospital or in the CHRS during the outbreak period were also screened and isolated.

TABLE 1
Services on floors of the Y and Z wings, Centre hospitalier régional du Suroît, September 1996

Floor	Y Wing	Z Wing
A	General and specialized medicine and surgery	
B	Surgery	
C	Surgery	Administration
D	General and specialized medicine	Administration
E	Pediatrics	Psychiatry
F	Intensive care, maternity, nursery, operating rooms	Extended care
G	Cafeteria, kitchen, pharmacy, laboratories	Extended care, Geriatric out-patient clinic
H	Emergency, observation room, radiology, outpatient clinic	Hemodialysis, out-patient clinic, sampling centre

TABLE 2
Targeted floors and results of the screening investigations following the identification of the first three cases

Date	Targeted Floors	No. of samples taken	No. of cases identified
1, 2, 3 Oct.	All floors (acute and extended care)	309	10
9, 10 Oct.	All acute-care floors	203	3
18, 21 Oct.	All floors where positive cases found	104	0
29, 30 Oct.	All floors where positive cases found	119	1
11 Nov.	All floors where positive cases found	74	0
2 Dec.	Entire floor adjacent to isolation area	30	0
Sept.-Dec.	Screening upon admission	268	3
TOTAL		1,107	17

in the same way. Table 2 describes the results of the screening investigations.

Environmental samples were also taken at various locations inside and outside the hospital rooms. Table 3 describes the results of the sampling. Hospital staff members were not included in the screening.

To determine the risk factors associated with VRE carriers, a descriptive study of the 20 cases was carried out through a systematic collection of information. A positive case was defined as anyone who had been hospitalized during the period being studied and found positive for VRE from a rectal swab or any other clinical specimen taken between September and December 1996. A standard questionnaire was used to collect data from medical files, hospital computer files, and from interviews with involved patients and nursing and medical staff. The collected information included demographic data, medical histories, and data from the current hospitalization (development of the disease, medication administered, operations, treatment, and duration of the stay). The movements of cases from room to room were pieced together. Because some cases had multiple recent admissions, their lengths of stay and movements were studied assuming that the outbreak began in mid-August. In addition, any possible transfers of cases or contacts during the previous year from a hospital outside of Quebec to the CHRS were documented.

Rectal swabs and environmental samples were usually cultured in enterococcosal agar (occasionally in enterococcosal broth), with 6 mg/L of vancomycin added and incubated at 35°C for 72 hours. A colony was identified as VRE when the isolate formed small

chains of gram-positive cocci, was catalase negative, pyrrolidonyl arylamidase positive, bile-esculin positive, and grew in 6.5% NaCl. The presence or absence of a yellow pigment was noted. Motility was verified by microscopic examination. Non-pigmented and immobile isolates were identified as *Enterococcus faecium* by the LSPQ. Presumed resistance to vancomycin was confirmed by growth at 35°C after 24 hours on brain-heart infusion (BHI) agar with 6 mg/L of vancomycin added and by E test. Minimum inhibitory concentrations (MICs) for ampicillin, vancomycin, and teicoplanin were then obtained by microdilution, according to criteria set out by the National Committee for Clinical Laboratory Standards. BHI agar with 500 mg/L of gentamycin and 2,000 mg/L of streptomycin added, respectively, was used to detect high-level sensitivities to these antibiotics. A nitrocephin disk was used to determine the presence of β -lactamase. The genomic study of the strains was carried out by the LSPQ using pulsed-field gradient gel electrophoresis (GGE). Van A, Van B, or Van C genes were determined by hybridization performed in the molecular microbiology laboratory of the Centre hospitalier de l'Université Laval, Québec.

Results

Between 3 September and 2 December 1996, 20 cases of VRE (*E. faecium*) colonizations were identified at the CHRS. The first two cases presented with positive cultures from clinical wound and urine specimens, respectively. The 18 other cases presented with positive cultures from rectal swabs. Table 4 summarizes the demographic and clinical data of the 20 cases.

The cases involved 13 women and seven men. The average age was 72 years (median: 78 years), ranging from 19 years to 95 years of age. Sixteen cases (80%) presented with comorbidity; seven cases (35%) involved more than three chronic systemic disorders. Five cases were taking corticosteroids: two habitually and three at prescribed times. None had had an organ transplant nor were on dialysis.

During their hospitalizations, 18 cases (90%) had received antibiotics and eight (40%) more than two types of antibiotics. Only one case received vancomycin. The average number of days

of hospitalization of the VRE-colonized cases (from the beginning of the outbreak to the discovery of the carrier state of each patient) was 17 days, ranging from 3 to 46 days.

A study of the rooms occupied by the 20 cases and their movements showed certain epidemiologic links without, however, fully explaining the means of transmission. All cases spent time in the emergency department ranging from a few hours to 48 hours and occupied various areas. Most of them spent some time in the observation room which contained eight stretchers; these stretchers were not assigned to a specific location. No other direct link was

TABLE 3
Results of environmental sampling

Environmental sampling	No. of samples taken	No. of positive samples and location
Inside of rooms:		
Rooms on floor A	98	4 (chest of drawers, telephone, toilet, mattress cover)
Rooms on floor B	15	0
Rooms on floor C	47	0
Outside of rooms:		
Lab equipment	4	0
X-ray equipment	3	0
Electronic thermometers	29	0

TABLE 4
Demographic and clinical data of cases colonized by VRE

Case no.	Age	Sex	Date sample taken	Diagnosis upon admission	Risk factors leading to VRE colonization		
					Comorbidity	Immunosuppression	Antibiotic therapy
1	80	F	3/9	Shoulder dislocation	x	x	xx
2	84	F	10/9	Cellulitis upper arm	x		x
3	19	F	27/9	Crohn's disease	x	x	xx
4	42	M	1/10	Appendicitis			xx
5	79	M	1/10	Weight loss	x		x
6	74	F	1/10	Abdominal pain			x
7	72	M	1/10	Cholecystitis			
8	73	F	1/10	Neoplasia of uterus	x		xx
9	84	F	2/10	Neoplasia of the vagina	x		x
10	95	F	2/10	Loss of independence	x		x
11	76	F	2/10	Decompensated COPD	x	x	x
12	79	F	9/10	Pneumonia	x		x
13	91	F	3/10	Acute pulmonary edema	x		xx
14	90	F	9/10	Decompensated COPD	x		xx
15	93	M	2/10	Pneumonia			x
16	82	M	9/10	Weight loss	x		xx
17	62	M	24/10	Decompensated COPD	x	x	xx
18	54	M	29/10	Decompensated COPD	x	x	xx
19	44	F	13/11	Incisional hernia	x		x
20	64	F	28/11	Plantar ulcer	x		x

xx = Administration of more than two antibiotics
COPD = Chronic obstructive pulmonary disease

found. Ruling out the emergency department, the cases occupied between one and eight different rooms before the discovery of the VRE carrier state. Only three spent time in intensive care.

Figures 1 and 2 show examples of the analysis of case movements on Floors A and D, respectively. The boxes indicate the duration of hospitalization for each case. Some cases have more than one box, indicating separate hospitalizations. The shaded area indicates the duration of hospitalization on the floor that was analyzed. The unshaded area indicates the duration of hospitalization when the case was located elsewhere in the hospital. Open boxes indicate that the case was still hospitalized at the end of October.

Room numbers are indicated in the shaded areas. The rooms were numbered according to their geographic proximity. An asterisk indicates the date when the first positive sample was taken. Two cases (19 and 20) were tested as outpatients following hospitalization; this is indicated by a set of three dots at the right of the figures. The dates of their first positive samples were 13 and 28 November 1996. On floor A, one can see that room 1, which contained four beds, was shared simultaneously or successively by four of the cases. On floor D, rooms 2 and 8 were each shared by three cases. An analysis of these movements explains, in part, the chain of transmission.

Case examinations and treatment upon hospitalization were analyzed; the only ones common to more than two-thirds of the cases were the insertion of intravenous catheters, the administration of antibiotics, and pulmonary x-rays.

None of the 20 VRE-colonized cases had been hospitalized in the United States or in another Canadian province. All of the transfers for the preceding year from hospitals outside of Quebec to the CHRS were examined. No link was found between such transfers and the outbreak. However, 2½ weeks and 3 months following the start of the outbreak, at least two university hospitals in the Montreal region experienced outbreaks, respectively. In one of these, the VRE strains were identified as the same as those in the CHRS outbreak. Even though the movements of patients between the CHRS and other Montreal-area hospitals were not systematically tracked, transfers for specialized examinations and treatment occurred regularly.

Due to difficulties in obtaining information, hospital staff members and equipment were not included in the investigation. Nurses assigned to one area of a floor would frequently work on the entire floor during their shift. Some would work various shifts on different floors. Other hospital staff, such as physicians and respiratory therapists, moved from one floor to another on any given day. Some equipment (e.g. thermometers, solution pumps and rods, and commodes) was shared among patients without always being disinfected after use; no written records were kept regarding the use of such equipment.

All of the positive VRE cultures taken from patients and from the environment were identified as ampicillin-teicoplanin-vancomycin-resistant *E. faecium* (vancomycin E test MIC > 250 mg/L and > 64 mg/L in microdilution). Moreover, the strains were resistant to a high concentration of gentamycin but remained sensitive to a high concentration of streptomycin. The strains

Figure 1
Cases on floor A in relation to lengths of stay and movements from room to room

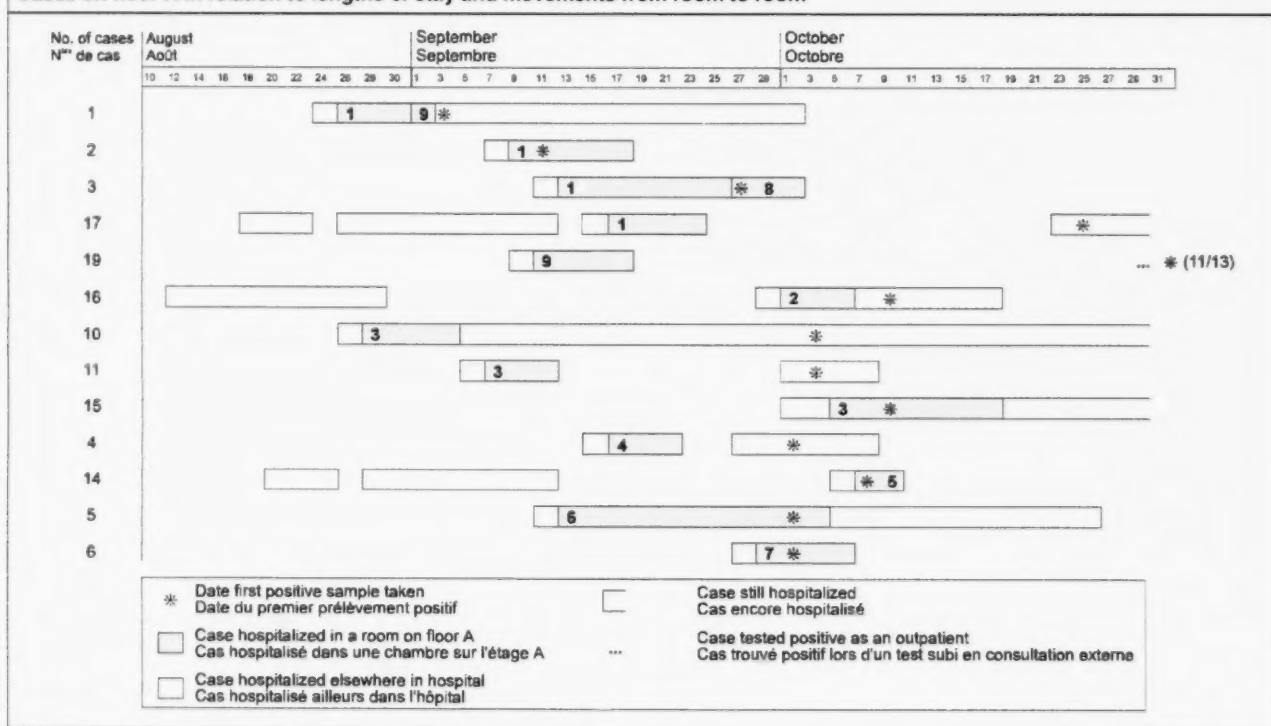
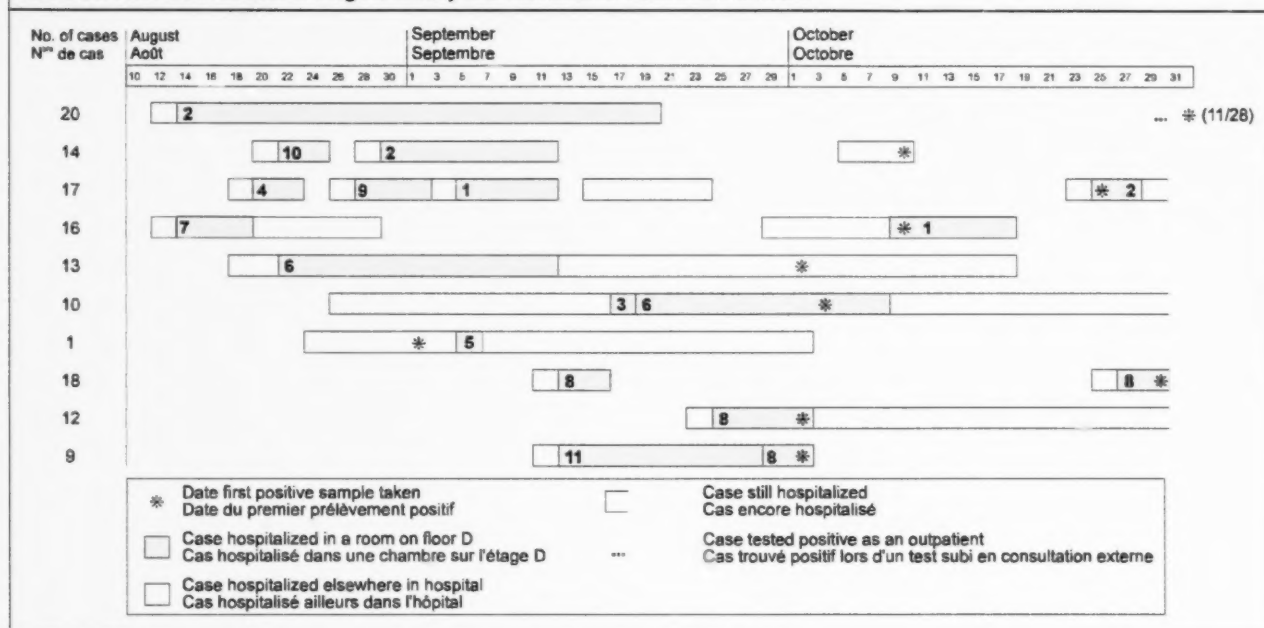


Figure 2
Cases on floor D in relation to lengths of stay and movements from room to room



produced no β -lactamase. A genotypic study showed that the resistance to vancomycin had been conferred by the Van A gene. Pulsed-field GGE indicated that the strains belonged to the same bacterial clone.

Intervention

Following the identification of the first VRE-colonized case, preventive and control measures were implemented to check the spread of this multiresistant bacteria in the hospital and in the community at large. A systematic screening of all patients at risk for colonization was set up as indicated above. Cases were isolated in single rooms with private bath or, less frequently, were paired with other cases. Isolation procedures included wearing gloves and long-sleeved gowns upon entering the room and using antibacterial soap for washing hands; these precautions applied to both hospital staff and visitors. The use of thermometers, stethoscopes, and other medical equipment was limited as much as possible to the cases only. Any equipment that could not be limited to the use of a single case was disinfected when taken from the room. Part of one floor was devoted solely to the care of cases. Hospital staff were assigned only to this isolation area. The contaminated rooms were cleaned and disinfected daily while cases were present, and a terminal disinfection was thoroughly performed.

Information sessions were held for hospital staff and community members. A member of the hospital infection prevention team met with individual patients and their families. A leaflet containing general information on VRE and describing control measures was distributed to all patients hospitalized during this period.

Although vancomycin prescriptions were not formally restricted during the outbreak, only hospital microbiologists prescribed this antibiotic and then only for accepted indications.

All of the above precautions resulted in the control of the spread of VRE in the hospital. As of 29 October 1996, no new cases were discovered. However, in January 1997 (3 months following the outbreak), the spouse of one of the cases was admitted to the CHRS. Since, this familial link only became known one week following hospitalization, the spouse was screened only at that time. She was found colonized by VRE. A new colonization outbreak occurred. Between January and July 1997, 42 cases were found; 24 of these were on floor D and 15 on floor B. There were no cases of infection. The same measures were applied.

Discussion

This first outbreak of VRE in Quebec alerted us to the fact that the province was no longer immune to the problem. The report of cases first breaking out in a medium-sized hospital without university affiliation in a particular region is rather unusual⁽²⁾. However, this could be explained by the frequent transfers between this particular hospital and larger ones in the Montreal area offering tertiary care, the relative ease with which VRE is transmitted from one patient to another, and the lack of active surveillance of the carrier state of VRE in the region.

The descriptive study points to certain known risk factors which can lead to VRE colonization: severe underlying disease, immunosuppression, multiple antibiotic therapy, and long-term hospitalization^(4,5). A number of transmission mechanisms were also revealed: sharing a room, health-care floor, and various medical equipment.

On the other hand, confirmation of these risk factors and transmission mechanisms would have required a control case study. This was not done for two main reasons: first, no new risk factor was identified in the descriptive study, and second, the

transfer of cases and the use of medical equipment was not sufficiently well documented to implement a control case study.

Finally, it should be noted that, despite systematic surveillance of enterococcal sensitivity on all clinical specimens at the CHRS during the year prior to the outbreak, six health-care floors had already been affected by the problem by the time the initial cases came to light. A screening limited to only those patients occupying the same rooms or floors as the initial cases would not have been sufficient to determine the scope of the outbreak.

Following the outbreak, the United States Centers for Disease Control and Prevention's voluntary VRE surveillance program, proposed in September 1995⁽¹⁾, has been reinforced in all hospitals in Quebec. In addition, prevention and control measures have been suggested for hospitals, long-term care facilities, rehabilitation centres, and home-care services which may also have to face cases of VRE colonization⁽⁶⁾. Such measures could possibly help to limit the spread of this bacteria in Quebec and in the rest of Canada.

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International Notes

PROGRESS TOWARDS ELIMINATION OF MEASLES IN THE AMERICAS WHO Expanded Programme on Immunization

In 1994, the countries in the WHO Region of the Americas established the goal of measles elimination by the year 2000. To achieve this goal, the Pan American Health Organization (PAHO) has developed a measles elimination strategy.

The PAHO measles elimination strategy aims to achieve and maintain very high levels of measles immunity in infants and children, and detect all chains of transmission of measles virus through careful surveillance. The strategy includes three vaccination components. First, a one-time "catch-up" measles vaccination is conducted with the aim to vaccinate all children 9 months through 14 years of age, regardless of measles disease history or vaccination status. Second, efforts are directed at

6. Groupe de travail sur les entérocoques résistants à la vancomycine. *Mesures de contrôle et de prévention des infections à entérocoques résistants à la vancomycine au Québec*. Québec, Québec: Ministère de la Santé et des Services sociaux du Québec, March 1998. In press.

Source: A Fortin, MD, F Milord, MD, M Guay, MD, *Direction de la santé publique de la Régie régionale de la santé et des services sociaux de la Montérégie, Saint-Hubert*; MA d'Halewyn, MSc, *Laboratoire de santé publique du Québec, Sainte-Anne-de-Bellevue*; P Vigeant, MD, G Leblanc, MAP, *CHRS, Valleyfield, Québec*.

Editorial Comment

The report of the first vancomycin-resistant enterococci VRE outbreak in Quebec, described above, is significant in that the colonized patients were elderly and had not received health-care outside of Quebec. The VRE strain in the medium-sized, regional hospital near Montreal was the same as the VRE strain found in a university hospital in Montreal. Possible mechanisms of transmission included staff, patient(s), and equipment. The infection control measures implemented are described.

Surveillance of enterococcal sensitivity on all clinical specimens indicated that six health-care floors had been affected by the time the initial cases were found. Infection control measures taken at the *Centre hospitalier régional du Suroît* were congruent with recommendations made by Health Canada in *Infection Control Guidelines: Preventing the Spread of Vancomycin-Resistant Enterococci (VRE) in Canada*⁽¹⁾. These include screening of patients at risk of VRE infection or colonization, using a single room with a private bathroom for VRE-colonized patients, educating patients and family members, wearing gloves and gowns by health-care personnel entering the room of the patient in isolation, washing hands with an antiseptic agent, dedicating the use of equipment to the colonized patient only, cleaning and disinfecting equipment removed from the isolation room, and cleaning and disinfecting environmental surfaces that may have been contaminated.

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1. Health Canada. *Infection control guidelines preventing the spread of vancomycin-resistant enterococci (VRE) in Canada*. CCDC 1997;23S8:1.1-1.16.

strengthening infant immunization through routine vaccination services ("keep-up") in order to maintain the interruption of measles virus circulation. If high coverage is achieved and maintained, the risk of an infant being exposed to measles virus is low and the age at which routine measles vaccination is administered can be safely increased from 9 to 12 months, thus providing an increase in vaccine effectiveness. Efforts are made to achieve 90% coverage in each successive birth cohort. Third, periodic "follow-up" vaccination campaigns are conducted targeting all children 1 to 4 years of age. In fact, since measles vaccine is < 100% effective and universal vaccination coverage is rarely achieved, there will be an accumulation of susceptible infants and children over time, increasing the risk of a measles

outbreak should the virus be introduced. The interval between "follow-up" campaigns is determined by the vaccination coverage obtained through routine vaccination services, but in practice, should be conducted at least every 4 years.

Surveillance is a critical component of PAHO's measles elimination strategy. Efforts have been made to improve measles surveillance throughout the Region, including the laboratory investigation of suspected measles cases.

Every country in the Region, with the exception of the United States of America and several French and Dutch Caribbean territories, conducted some form of measles "catch-up" campaign between the years 1987 and 1994; the coverage achieved in these campaigns was 94% region-wide, and the range in country-specific coverage was 71% to 99%. In addition, there has been a progressive increase in routine measles vaccination coverage among infants from 42% in 1980 to 86% in 1996. In 1996, 27 (57%) of 47 countries/areas achieved a coverage of at least 90% in their routine vaccination services and only 5 (11%) presented a coverage below 80%. Since 1994, 26 (55%) of the 47 countries/areas have also conducted follow-up vaccination campaigns.

Following the implementation of the strategies outlined above, there has been a marked reduction in the annual number of reported measles cases in the Region. In 1996, the all-time record low of 2,109 confirmed measles cases was reported from the countries of the Americas. Of the 47 countries/areas which provide measles surveillance data to PAHO on a weekly basis, 29 (61%) reported zero confirmed measles cases and 38 (80%) reported 10 or fewer cases. Most of the Region was free of measles virus circulation during 1996.

In 1997, however, there was a resurgence of measles in the Region, especially in São Paulo State in Brazil. Provisional data received at PAHO through February 1998 indicate a total of 88,485 suspected measles cases reported from the countries in the Americas. Of these, 27,635 (31%) have been confirmed, 33,120 (37%) have been discarded, and 27,730 (31%) remain under investigation.

Of the total confirmed cases, 26,919 (97%) were confirmed by laboratory testing or epidemiologic linkage to a laboratory-confirmed case and 716 (3%) were confirmed on clinical grounds alone, without laboratory investigation. Together, Brazil (26,348 confirmed cases) and Canada (570 confirmed cases) accounted for 97% of the total confirmed cases in the Region. Other countries/areas reporting > 10 confirmed measles cases during 1997 include the United States (135 cases), Paraguay (198 cases), Guadeloupe (116 cases), Argentina (96 cases), Chile (59 cases), Venezuela (27 cases), and Costa Rica (15 cases).

Of the total confirmed cases reported from Brazil, 20,186 (77%) were reported from São Paulo State – the only state in the country that did not conduct a "follow-up" measles vaccination campaign

in 1995. Most cases in this outbreak occurred in persons living in the greater São Paulo metropolitan area. Of the 19,322 confirmed measles cases reported from São Paulo State whose ages were recorded, 9,938 (51%) occurred in persons 20 to 29 years of age. The highest age-specific incidence rates were reported in infants < 1 year of age (456 cases per 100,000), young adults 20 to 29 years of age (156 cases per 100,000), and children 1 to 4 years of age (45 cases per 100,000). Twenty measles-related deaths were reported; 17 (85%) occurred in infants < 1 year of age. A detailed epidemiologic investigation is currently under way to determine specific risk factors for measles in São Paulo.

Canada reported a total of 570 confirmed measles cases during 1997. A large outbreak with over 300 cases occurred in a university community in British Columbia. Most cases occurred in young adults who had been previously vaccinated with one dose of measles vaccine. Genomic analysis of measles virus obtained from patients during this outbreak suggested that measles virus circulating in British Columbia was imported from Europe. Measles virus from the British Columbia outbreak spread to the neighbouring province of Alberta, where 245 cases were reported; most cases occurred in school-aged children who were previously vaccinated with one dose of measles vaccine.

The United States reported a provisional total of 135 confirmed measles cases during 1997. This is the lowest number of cases ever reported and is less than one-half the previous record low incidence of 309 cases in 1995. During an 8-week period, no indigenous measles cases were reported, suggesting an interruption of measles transmission. Fifty-seven (42%) of the reported cases were documented international importations, primarily from Europe and Asia.

Source: WHO Epidemiological Record, Vol 73, No 12, 1998.

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